



AP35518 (072396.0263)  
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Robbins *et al.* Customer No.: 21003  
Serial No. : 10/807,755 Examiner: Not Yet Assigned  
Filed : March 24, 2004 Group Art Unit: 1646  
For : A COMPACT SYNTHETIC EXPRESSION VECTOR  
COMPRISING DOUBLE-STRANDED DNA MOLECULES  
AND METHODS OF USE THEREOF

**INFORMATION DISCLOSURE STATEMENT**

I hereby certify that this paper is being deposited with the  
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June 24, 2004

Date

Rochelle K. Seide

Attorney Name

Rochelle K. Seide  
Signature

32,300

PTO Reg. No

June 24, 2004

Date of Signature

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Pursuant to 37 C.F.R. §§1.97 and 1.98, Applicants respectfully request that the documents listed below and on the accompanying PTO 1449 be considered by the Examiner and made of record in the above-referenced application. Copies of the listed documents are enclosed.

1. Martinez *et al.* Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi. Cell 2002;110:563-74;

2. Zeng *et al.* Both Natural and Designed Micro RNAs Can Inhibit the Expression of Cognate mRNAs When Expressed in Human Cells. *Mol. Cell* 2002;9:1327-1333;
3. Stanojevic and Young. A Highly Potent Artificial Transcription Factor. *Biochemistry* 2002;41:7209-7216;
4. Xia *et al.* siRNA-mediated gene silencing in vitro and in vivo. *Nature Biotech.* 2002;20:1006-10;
5. Matheos *et al.* Ku antigen, an origin-specific binding protein that associates with replication proteins, is required for mammalian DNA replication. *Biochim. Biophys. Acta.* 2002;1578:59-72;
6. Jacque *et al.* Modulation of HIV-1 replication by RNA interference. *Nature* 2002;418:435-438;
7. Opalinska and Gewirtz. Nucleic-acid therapeutics: basic principles and recent applications. *Nat Rev Drug Discov* 2002;1:503-14;
8. Gary Ruvkun. Glimpses of a Tiny RNA World. *Science* 2001;2294:797-799;
9. Robert Barstead. Genome-wide RNAi. *Curr. Opin. Chem. Biol.* 2001;5:63-66;
10. Phillip D. Zamore. RNA interference: listening to the sound of silence. *Nat. Struct. Biol.* 2001;8:746-750;
11. Fjose *et al.* RNA interference: mechanisms and applications. *Biotechnol. Annu. Rev.* 2001;7:31-57;
12. Zhao *et al.* Double-Stranded RNA Injection Produces Nonspecific Defects in Zebrafish. *Dev. Biol.* 2001;229:215-223;
13. Kassavetis *et al.* The RNA polymerase III transcription initiation factor TFIIIB participates in two steps of promoter opening. *EMBO J.* 2001;20:2823-2834;

14. Mark Lewandoski. Conditional control of gene expression in the mouse. *Nat. Rev. Genet.* 2001;2:743-755;
15. Reinhart *et al.* The 21-nucleotide let-7 RNA regulates developmental timing in *Caenorhabditis elegans*. *Nature* 2000;403:901-906;
16. Tavernarakis *et al.* Heritable and inducible genetic interference by double-stranded RNA encoded by transgenes. *Nat. Genet.* 2000;24:180-183;
17. Nakano *et al.* RNA Interference for the Organizer-Specific Gene Xlim-1 in *Xenopus* Embryos. *Biochem. Biophys. Res. Commun.* 2000;274:434-439;
18. Svoboda *et al.*, Selective reduction of dormant maternal mRNAs in mouse oocytes by RNA interference. *Development* 2000;127:4147-4156;
19. Ohkawa and Taira. Control of the Functional Activity of an Antisense RNA by a Tetracycline-Responsive Derivative of the Human U6 snRNA Promoter. *Human Gene Ther.* 2000;11:577-585;
20. Olejnik *et al.* Photocleavable aminotag phosphoramidites for 5'-termini DNA/RNA labeling. *Nucl. Acids Res.* 1998;26:3572-3576;
21. Wang *et al.* Plasmids for the in vitro analysis of RNA polymerase II-dependent transcription based on a G-free template. *Biochimica et Biophysica Acta* 1998;1397:141-145;
22. Tichelaar *et al.* In Vivo Expression of a Variant Human U6 RNA from a Unique, Internal Promoter. *Biochemistry* 1998;37:12943-12951;
23. Nyanguile *et al.* A nonnatural transcriptional coactivator. *Proc. Natl. Acad. Sci. USA* 1997;94:13402-13406;

24. Jacobs and Langland. When Two Strands Are Better Than One: The Mediators and Modulators of the Cellular Responses to Double-Stranded RNA. *Virology* 1996;219:339-349;
25. Berns and Giraud Adenovirus and Adeno-Associated Virus as Vectors for Gene Therapy. *Ann. N.Y. Acad. Sci.* 1995;772:95-104;
26. Alan E. Smith. Viral vectors in gene therapy. *Ann. Rev. Microbiol.* 1995;49:807-838;
27. Yang *et al.* Cellular and Humoral Immune Responses to Viral Antigens Create Barriers to Lung-Directed Gene Therapy with Recombinant Adenoviruses. *J. Virol.* 1995;69:2004-2015;
28. Izban *et al.* RNA Polymerase II Ternary Complexes May Become Arrested after Transcribing to within 10 Bases of the End of Linear Templates. *J. Biol. Chem.* 1995;270:2290-2297;
29. Krebs *et al.* The JC Virus Minimal Core Promoter Is Glial Cell Specific In Vivo. *J. Virol.* 1995;69:2434-2442;
30. Pan and Greenblatt. Initiation of Transcription by RNA Polymerase II Is Limited by Melting of the Promoter DNA in the Region Immediately Upstream of the Initiation Site. *J. Biol. Chem.* 1994;269:30101-30104;
31. Lee *et al.* The *C. elegans* Heterochronic Gene *lin-4* Encodes Small RNAs with Antisense Complementarity to *lin-14*. *Cell* 1993;75:843-54;
32. Richard C. Mulligan. The Basic Science of Gene Therapy. *Science* 1993;260:926-932;

33. Hubbell *et al.* Cyclic AMP mediates the direct antiproliferative action of mismatched double-stranded RNA. Proc. Natl. Acad. Sci. USA 1991;88:906-910;
34. Zaug *et al.* The Tetrahymena ribozyme acts like an RNA restriction endonuclease. Nature 1986;324:429-33;
35. Gelboin *et al.* Polyinosinic-Polycytidylic Acid Inhibits Chemically Induced Tumorigenesis in Mouse Skin. Science 1970;167:205-207;
36. Levy *et al.* Inhibition of tumor growth by polyinosinic-polycytidylic acid. Proc. Nat. Acad. Sci. USA 1969;62:357-361; and
37. Zeleznick *et al.* Treatment of Leukemic (L-1210) Mice with Double-Stranded Polyribonucleotides (33503). Proc. Soc. Exp. Biol. Med. 1969;130:126-128.

This submission does not represent that a search has been made or that no better art exists and does not constitute an admission that the listed documents are material or constitute "prior art." If the Examiner applies the documents as prior art against any claim in the application and Applicants determine that the cited documents do not constitute "prior art" under United States law, Applicants reserve the right to present to the Office the relevant facts and law regarding the appropriate status of the documents.

Applicants further reserve the right to take appropriate action to establish the patentability of the disclosed invention over the listed documents, should the documents be applied against the claims of the present application.

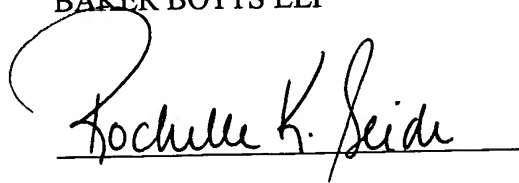
This Information Disclosure Statement is being filed before the mailing date of the first Office Action on the merits of referenced application. Therefore, Applicants do not believe that any fee is due in connection with the submission of this paper. However, if any fee is due, or if any overpayment has been made, the Commissioner is authorized

to charge any such fee or credit any overpayment, to our Deposit Account No. 02-4377.

Duplicate copies of this sheet are enclosed.

Respectfully submitted,

BAKER BOTTS LLP

A handwritten signature in cursive script, reading "Rochelle K. Seide", is written over a horizontal line.

Rochelle K. Seide  
Patent Office Reg. No. 32,300

Carmella L. Stephens  
Patent Office Reg. No. 41,328

Attorneys for Applicants

30 Rockefeller Plaza  
44th Floor  
New York, NY 10112-4498

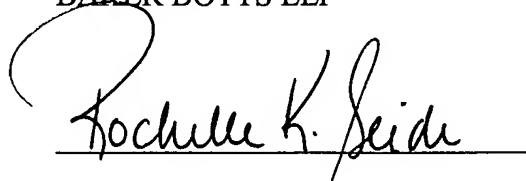
(212) 408-2626

to charge any such fee or credit any overpayment, to our Deposit Account No. 02-4377.

Duplicate copies of this sheet are enclosed.

Respectfully submitted,

BAKER BOTTS LLP

A handwritten signature in dark ink, reading "Rochelle K. Seide", is written over a horizontal line. The signature is fluid and cursive.

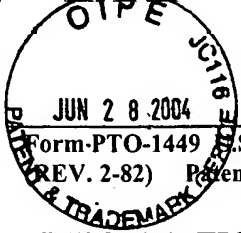
Rochelle K. Seide  
Patent Office Reg. No. 32,300

Carmella L. Stephens  
Patent Office Reg. No. 41,328

Attorneys for Applicants

30 Rockefeller Plaza  
44th Floor  
New York, NY 10112-4498

(212) 408-2626

Form-PTO-1449 U.S. Department of Commerce  
REV. 2-82) Patent and Trademark OfficeAtty. Docket No.  
AP35518 (072396.0263)Serial No.  
10/807,755**INFORMATION DISCLOSURE STATEMENT  
BY APPLICANT**  
(Use several sheets if necessary)Applicants  
Robbins *et al.*Filing Date  
March 24, 2004Group Art Unit  
1646**U.S. PATENT DOCUMENTS**

*Exam. Init.	Document No.	Date	Name	Class	Subclass	Filing Date if Appropriate

**FOREIGN PATENT DOCUMENT**

Document No.	Class	SubClass	Translator Yes No

**OTHER DOCUMENTS (including Author, Title Date, Pertinent Pages, Etc.)**

1.	Martinez <i>et al.</i> Single-Stranded Antisense siRNAs Guide Target RNA Cleavage in RNAi. Cell 2002;110:563-74.
2.	Zeng <i>et al.</i> Both Natural and Designed Micro RNAs Can Inhibit the Expression of Cognate mRNAs When Expressed in Human Cells. Mol. Cell 2002;9:1327-1333.
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10.	Phillip D. Zamore. RNA interference: listening to the sound of silence. Nat. Struct. Biol. 2001;8:746-750.

Examiner

Date Considered

\* Examiner: Initial citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not conformance and not considered. Include copy of this form with next communication to applicant.



<b>Form PTO-1449 U.S. Department of Commerce</b> <b>(REV. 2-82) Patent and Trademark Office</b>  <b>INFORMATION DISCLOSURE STATEMENT</b> <b>BY APPLICANT</b> <b>(Use several sheets if necessary)</b>	Atty. Docket No. AP35518 (072396.0263)	Serial No. 10/807,755
	Applicants Robbins <i>et al.</i>	
	Filing Date March 24, 2004	Group Art Unit 1646

11.	Fjose <i>et al.</i> RNA interference: mechanisms and applications. <i>Biotechnol. Annu. Rev.</i> 2001;7:31-57.
12.	Zhao <i>et al.</i> Double-Stranded RNA Injection Produces Nonspecific Defects in Zebrafish. <i>Dev. Biol.</i> 2001;229:215-223.
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	26.	Alan E. Smith. Viral vectors in gene therapy. <i>Ann. Rev. Microbiol.</i> 1995;49:807-838.
	27.	Yang <i>et al.</i> Cellular and Humoral Immune Responses to Viral Antigens Create Barriers to Lung-Directed Gene Therapy with Recombinant Adenoviruses. <i>J. Virol.</i> 1995;69:2004-2015.
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